REMARKS

I. Status Summary

Claims 1-8 are pending in the present U.S. patent application.

Claims 1-8 have been rejected under 35 U.S.C. §103(a) upon the contention that the claims are unpatentable over U.S. Patent No. 5,707,807 to Kato (hereinafter "Kato") in view of PCT International Patent Publication No. WO 99/41415 to Arbuckle et al. (hereinafter "Arbuckle").

Claims 1-8 also have been provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-39 and 95-98 of co-pending U.S. Patent Application Serial No 10/055,109 (hereinafter "the '109 Application").

Claim 1 has been amended herein. No new matter has been added. Reconsideration of the application in view of the amendment and remarks set forth herein below is respectfully requested.

II. Rejection under 35 U.S.C. § 103(a) over Kato in view of Arbuckle

Claims 1-8 have been rejected under 35 U.S.C. §103(a) upon the contention that the claims are obvious over Kato in view of Arbuckle. With regard to claims 1 and 4, the Patent Office asserts that Kato teaches a method for amplifying a population of polynucleotides by reverse transcribing an RNA population, digesting the resulting cDNA population with one or more restriction endonucleases having degenerative recognition or cleavage sequences, ligating the fragments to a series of adaptors, and amplifying the restriction fragments for 25 to 30 cycles. With regard to claims 3 and 5-8, the Patent Office alleges that Kato teaches a restriction endonuclease comprising a four-base cutter, use of a series of adaptors having a sequence complementary to overhangs, amplifying the restriction fragments using PCR, using the adaptors as priming sites for PCR, and detection of the PCR products using gel electrophoresis. The Patent Office concedes that Kato does not specifically teach amplifying restriction fragments for no more than 25 cycles or quantifying the restriction fragments. The

Patent Office contends that Arbuckle cures this deficiency by teaching a modified AFLP method that includes amplification of the restriction fragments for no more than 25 cycles and the quantitation of the amplified restriction fragments.

The Patent Office further alleges that it would have been *prima facie* obvious to one of ordinary skill in the art to modify the method of Kato with a step including the quantitation of the amplification products as taught by Arbuckle in order to enhance the specificity of detecting a target amplification product to provide an efficient DNA fingerprinting method. More specifically, the Patent Office contends that one of ordinary skill in the art would have been motivated to combine the teachings of Arbuckle with the method of Kato to arrive at the presently claimed subject matter because Arbuckle explicitly teaches that the use of touchdown PCR with no more than 25 cycles solves problems regarding annealing temperatures of different adapter-primers and aids in the specific quantitation of amplified products for the purpose of efficient detection of DNA fingerprinting patterns. Thus, the Patent Office argues that one of ordinary skill in the art would have had a reasonable expectation of success that "amplification for no more than 25 cycles and quantitation of the amplified restriction fragments would result in enhancing the specificity of detection of DNA fingerprinting." See Official Action, page 5.

After careful consideration of the rejections and the Patent Office's bases therefor, applicants respectfully traverse the rejections and submit the following remarks.

Initially, applicants submit that claim 1 has been amended herein to recite that that the amplifying of step (d) for no more than 25 cycles produces an amplified subset of restriction fragments that is linearly representative of the RNA of step (a). Support for this amendment can be found in the specification as filed at page 25, lines 27-28. Further, claim 1 has been amended to clarify that the quantitation of step (e) relates to the amplified subset of restriction fragments recited in step (d). Support for this amendment can be found in the specification as filed at page 7, lines 1-6; page 8, lines 6-9; and page 9, lines 4-5.

Applicants respectfully submit that to establish a *prima facie* case of obviousness, all the claim limitations must be taught or suggested by the prior art references when combined. *See In Re Royka* 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Further, the motivation to make the claimed combination and a reasonable expectation of success must both be found in the prior art. *See In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991); and Manual of Patent Examining Procedure, (M.P.E.P) § 2143.

The Patent Office has acknowledged that Kato does not specifically teach amplifying restriction fragments for no more than 25 cycles and quantitation of amplified restriction fragments. *See* Official Action, middle of page 4.

With regard to the Patent Office's contention that Arbuckle teaches amplification using no more than 25 cycles, applicants note that the cited section of Arbuckle, page 21 lines 18-21, in describing "touchdown" PCR, states, "... the initial programmed annealing temperature of the cycling profile was 2 °C higher than the Tm of the *Mu*-TIR-derived primer." Applicants note that this statement appears to describe the annealing temperature of a first PCR amplification cycle. The passage continues, "In each of the next 7 cycles, the programmed annealing temperature was reduced by 1 °C. For the next 25 cycles the programmed annealing temperature remained at ((Tm *Mu*-TIR primer +2)-7)." *See* Arbuckle, page 21, lines 21-23, emphasis added. Thus, it appears that the PCR method described on page 21 of Arbuckle includes a total of 33 cycles of PCR amplification. Therefore, applicants submit that Arbuckle does not describe using no more than 25 cycles, as recited in claim 1 of the instant application.

Moreover, applicants respectfully submit that Arbuckle does not teach quantitation of the amplification products. In general, Arbuckle appears to be directed at a method for the rapid isolation and identification of transposable element-tagged genes. Arbuckle describes methods for providing a labeled amplification product to aid in identifying electrophoresed bands of an amplified product (Arbuckle, page 16, lines 9-12). Arbuckle also describes that the amplified product may be isolated and sequenced. However, Arbuckle makes no mention of quantifying the amplified product.

Stated another way, Arbuckle does not discuss measuring or estimating the concentration or the number of copies of an amplified subset of restriction fragments or of any amplified product.

Finally, Arbuckle does not teach producing an amplified subset of restriction fragments that is linearly representative of the RNA population from which the subset of restriction fragments is based. In the TAIL-PCR method described by Arbuckle "*Mu*-containing sequences are preferentially and geometrically amplified over nontarget sequences", thus "enriching for *Mu*-containing products". *See* Arbuckle page 14, line 23 to page 15, line 23. The enriched amplification products from the TAIL-PCR process are then further amplified using "touchdown" PCR. Thus, applicants submit that, at best, the methods described by Arbuckle aid in the detection of a sequence of interest. In contrast, the specification of the present U.S. patent application discloses that "amplification is restricted to <25 cycles in order to achieve the linear representation of the mRNA concentration." *See* page 25, lines 27-28. Claim 1 has been amended herein to recite that the amplification of step (d) produces an amplified subset of restriction fragments that is linearly representative of the RNA population of step (a). Thus, applicants respectfully submit that Arbuckle and Kato, either alone or in combination, do not teach all the elements of claim 1.

Applicants also respectfully traverse the Patent Office's contention that one of ordinary skill in the art would be motivated to combine the teaching of Arbuckle with Kato to arrive at the presently claimed subject matter, *i.e.* that Arbuckle teaches that the use of touchdown PCR with no more than 25 cycles "aids in specific quantitation of amplified products for the purpose of efficient detection of DNA fingerprinting pattern." *See* Official Action, page 5.

First, as discussed hereinabove, it is believed that Arbuckle in fact does not teach PCR for no more than 25 cycles. Nor does Arbuckle teach the quantitation of an amplified subset of restriction fragments. Further, by providing an enriched population of amplified products, the methods described in Arbuckle specifically do not provide for the linear amplification of a subset of restriction fragments, which would be necessary

for ensuring that the amplified subset of restriction fragments accurately reflects the relative composition of a starting RNA population. Thus, applicants respectfully submit that Arbuckle does not provide the motivation or the expectation of success for producing or quantitating an amplified subset of restriction fragments that is linearly representative of an RNA population, as recited in claim 1 of the presently disclosed subject matter.

Therefore, applicants respectfully submit that the Patent Office has not demonstrated that it would have been *prima facie* obvious to one of ordinary skill in the art to combine the teachings of the cited references to arrive at the presently claimed subject matter, as the cited references, either alone or in combination, do not teach each and every element of claim 1. Further, the applicants submit that there is no motivation to combine the cited references or a reasonable expectation of success that such a combination would provide the method of claim 1. Accordingly, applicants respectfully request that the rejection of claim 1 over Kato in view of Arbuckle under 35 U.S.C. § 103(a) either alone or in combination be withdrawn, and that claim 1 be allowed at this time.

Claims 2-8 depend from claim 1 and, therefore, include the elements of claim 1. Thus, as claim 1 is believed to be patentable over Kato and Arbuckle, applicants respectfully submit that dependent claims 2-8 are patentable over Kato and Arbuckle and request that the rejection of the dependent claims 2-8 under 35 U.S.C. § 103(a) be withdrawn. Further, applicants respectfully request that claims 2-8 be allowed at this time.

III. Obviousness-Type Double Patenting Rejection

Claims 1-8 have been provisionally rejected based upon the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-39 and 95-98 of the copending '109 Application. The Patent Office alleges that claims 1-8 of the present application fall within the scope of the claims of the '109 Application. The Patent Office asserts that the only variation in the instant subject matter and that of the

co-pending application is that the co-pending application does not disclose amplification of restriction fragments for no more than 25 cycles. The Patent Office contends that Arbuckle teaches amplification using no more than 25 cycles and that it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to modify the method of the co-pending application with the step of including amplification for no more than 25 cycles as taught by Arbuckle for the purpose of "enhancing the specificity of detecting a target amplification product" (*See* Official Action, page 7). Further, the Patent Office contends that one skilled in the art would be motivated to combine the method taught by the co-pending application with amplification using no more than 25 cycles as taught by Arbuckle because "Arbuckle teaches that touchdown PCR with no more than 25 cycles aids in specific quantitation of amplified products." *See* Official Action, bottom of page 7.

Initially, Applicants note that the '109 Application has issued as U.S. Patent No. 6,727,068. The claims cited by the Patent Office from the application, claims 1-39 and 95-98, appear to correspond to claims 1-39 and 40-43 of the issued patent, respectively.

After careful consideration, applicants respectfully traverse the rejection. As argued above, Arbuckle does not disclose amplification of a subset of restriction fragments for no more than 25 cycles. Furthermore, applicants submit that one of skill in the art would not be motivated to combine the teaching of Arbuckle with the disclosure or the claims of the '109 Application to provide the currently claimed method, because, as discussed above, Arbuckle does not teach quantitation of amplified products. Arbuckle at best teaches a method for preferentially amplifying and detecting a specific target sequence. More specifically, Arbuckle describes identifying a band of a given amplified product on a gel, and isolating, sequencing, and cloning that product. Arbuckle does not teach measuring the amount of an amplified product. Also, because the amplification methods described by Arbuckle would not provide a linearly representative amplified subset of restriction fragments, one of skill in the art would not be motivated use the teaching of Arbuckle with the disclosure or claims of the '109

Application to quantify the amplified subset of restriction fragments, as is recited in claim 1 of the subject application. Therefore, the applicants respectfully submit that one of skill in the art would not be motivated to combine the cited references.

Applicants respectfully submit that the Patent Office has not demonstrated that it would have been *prima facie* obvious for one of skill in the art to combine the disclosure of nor the claims of the '109 Application and Arbuckle to provide the method of claim 1. Further, the combined references do not contain each and every element of claim 1. Applicants respectfully request that the rejection of claim 1 under the judicially created doctrine of obviousness-type double patenting be withdrawn, and that claim 1 be allowed at this time.

As claims 2-8 are dependent from claim 1 and include the elements of claim 1, applicants also respectfully request that the rejection of claims 2-8 be withdrawn and that claims 2-8 be allowed at this time.

CONCLUSIONS

In light of the above amendments and the remarks presented hereinabove, it is respectfully submitted that claims 1-8 are in proper condition for allowance, and such action is earnestly solicited.

If any minor issues should remain outstanding after the Examiner has had an opportunity to study the Amendment and Remarks, it is respectfully requested that the Examiner telephone the undersigned attorney so that all such matters may be resolved and the application placed in condition for allowance without the necessity for another Action and/or Amendment.

Serial No.: 09/896,324

DEPOSIT ACCOUNT

The Commissioner is hereby authorized to charge any deficiencies or credit any overpayments associated with the filing of this correspondence to Deposit Account Number **50-0426**.

Respectfully submitted,
JENKINS, WILSON, TAYLOR & HUNT, P.A.

Date: 03/08/2006

By: Arles A. Taylor, Jr.
Registration No. 39,395

Customer No.: 25297